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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,295	08/04/2006	**Michel Chartrain**	21502P	8419

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EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,295	CHARTRAIN ET AL.	
	Examiner	Art Unit	
	Michele K. Joike	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,9 and 40-56* is/are pending in the application.

4a) Of the above claim(s) *51-55* is/are withdrawn from consideration.

5)☒ Claim(s) *56* is/are allowed.

6)☒ Claim(s) *1, 3, 9, 40, 41, 44-50* is/are rejected.

7)☒ Claim(s) *42 and 43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed October 8, 2009. Claims 1, 3, 9 and 40-56 are pending in the instant application. Any rejection of record in the previous Office Action, mailed June 10, 2009 that is not addressed in this action has been withdrawn.

Because this Office Action introduces new rejections other than those set forth in the previous Office Action, and are not necessitated by amendment, this Office Action is Non-Final.

Newly submitted claims 51-55 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The claims are drawn to a process for production of plasmid DNA comprising duplicate plating. This is a step and limitation not previously presented.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 51-55 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 44 and 48, the plasmid copy number of potentially highly productive clonal subtypes is determined by cultivation. How is plasmid copy number determined by merely cultivating the subtypes?

In claim 47, the potentially highly productive clonal subtypes are purified by isolating colonies from a second type of agar. It is unclear how isolating colonies will purify them. Also at what point are the subtypes plated on a second agar?

Response to Arguments

Applicant's arguments, see pages 4 and 5, filed October 8, 2009, with respect to the rejection(s) of claim(s) 1, 2, 4, 11 and 12 under 35 U.S.C. 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of newly found prior art reference, Voziyanov et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been

> obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 40, 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cress et al in view of Korz et al and in further view of Voziyanov et al.

Cress et al (IDS ref., pp. 635, 636, 638 and 639) teach a method for producing plasmid by isolating chromosomal mutants of E. coli that maintain higher levels of an F' plasmid and cultivating them. The mutants were initially detected by selecting for increased lactose fermentation. The reference teaches that a well-established approach to detecting mutants with altered plasmid replication is to examine the bacterial population for increased expression of plasmid-linked genes. The mutants had 2-7 times more plasmids than unselected strains. The cells were cultured at 30°C for 24-30 hrs. Although, the cells were grown for 30 hrs, and not 48 hrs, one of ordinary skill in the art would

know that time can be optimized depending on the strain and medium used for growth.

A. Optimization Within Prior Art Conditions or Through Routine Experimentation

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

However, Cress et al do not teach fed batch fermentation for culturing the cells or selecting potentially highly productive clonal subtypes colonies that represent a minor component by observing phenotype heterogeneity.

Korz et al (IDS ref., pp. 59-60) teach a fed batch process for high cell density cultivation of E. coli. Glycerol was the carbon source, and the medium also contained KH_2PO4, $(NH_4)_2HPO_4$ and $MgSO_4.7H_2O$.

Additionally, as evidenced by microbelibrary.org, E. coli cells grown on blood agar are phenotypically gray.

Voziyanov et al (Nuc. Acid Res. 30(7): 1656-1663, 2002, see entire paper) teach a dual reporter screen where the colonies are phenotypically white, blue or red depending on the plasmid content. As shown in figure 2, red colonies make up the minor component of the colonies on the plate. Since the red colonies contain a different plasmid than the white and blue colonies, these colonies will have a higher plasmid copy number of that plasmid as compared to the other subtypes of the E. coli strain. The plasmids from the red colonies were isolated.

The ordinary skilled artisan would have been motivated to combine the teachings of Cress et al teaching for producing plasmid by isolating chromosomal mutants of E. coli that maintain higher levels of an F' plasmid and cultivating them with the teachings of Korz et al teaching fed batch fermentation with the teachings of Voziyanov et al because Korz et al state that E. coli is an important host organism for recombinant protein, and to maximize the volumetric productivities of bacterial cultures it is important to grow E. coli to high cell concentrations, like in fed batch fermentation. It would have been obvious to one of ordinary skill in the art because Cress et al teaches that the method has been successful to isolate mutants that harbor plasmids at increased levels. Additionally Voziyanov et al teach that simultaneous selection for and selection against based on phenotypic observations are beneficial for functional selection. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to

the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cress et al, Korz et al and Voziyanov et al as applied to claims 1, 40, 41 above, and further in view of Mason et al.

Cress et al, Korz et al and Voziyanov et al teach all of the limitations as described above. However, they do not teach use of DH5.

Mason et al (IDS ref.) teaches using DH5α cells and increasing copy number of plasmids.

The ordinary skilled artisan, desiring to use DH5, would have been motivated to combine the teachings of Cress et al teaching for producing plasmid by isolating chromosomal mutants of E. coli that maintain higher levels of an F' plasmid and cultivating them with the teachings of Korz et al teaching fed batch fermentation and Mason et al because Mason et al state that DH5α cells help avoid possible secondary metabolic stress imposed by amino acid auxotrophy. It would have been obvious to one of ordinary skill in the art because Mason et al teach that DH5α influences plasmid copy number and overall gene expression. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cress et al, Korz et al, Voziyanov et al and Mason et al as applied to claims 1, 3, 40, 41 above, and further in view of Kongo et al.

Cress et al, Korz et al, Mason et al and Voziyanov et al teach all of the limitations as described above. However, they do not teach use of Medium C.

Kongo et al (Food Microbio. and Safety 68(9): 2742-2476, 2003) teaches using Medium C for growing bacteria.

The ordinary skilled artisan would have been motivated to combine the teachings of Cress et al teaching for producing plasmid by isolating chromosomal mutants of E. coli that maintain higher levels of an F' plasmid and cultivating them with the teachings of Korz et al teaching fed batch fermentation, Voziyanov et al, Kongo et al and Mason et al because Kongo et al state that Medium C caused superior growth. It would have been obvious to one of ordinary skill in the art because Kongo et al teach that nitrogen bases have growth-promoting effects. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

Claims 42 and 43 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 56 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 10:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michele K. Joike/
Primary Examiner, Art Unit 1636

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